The effect of ghrelin On sex hormones in infertiled men

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Abstract:

The present study was designed to evaluate the effect of ghrelin on sex hormones, follicle stimulating hormones, luteinizing hormones, Testosterone, and prolactin in infertiled men. Abnormal spermatogenesis is often associated with altered serum gonadotropins and testosterone. follicle stimulating hormones, luteinizing hormones, and testosterone levels They were estimated in 50 infertiled men. Results showed statistically significant increase ($p< 0.05$) in the mean of ghrelin, follicle stimulating hormones, luteinizing hormones, Thyroid stimulating hormones, Prolactin, fasting blood sugar , Triglyceride, High density lipoprotein, Very low density lipoprotein, in all the studied infertiled males patients when compared with the fertiled control (n=20). In addition there was no significant differences in the levels of testosterone , Cholesterol ,and Low density Lipoprotein, between the infertiled and fertiled men.

Key words*:* Ghrelin, FSH, LH, Testosterone, prolactin, TSH, lipid profile, FBS.

Introduction:

Ghrelin is a unique 28 amino acids peptide containing an *n*-octanoyl group on the serine in position 3[(1)].Ghrelin is the only known peptide hormone modified by a fatty acid. Ghrelin is synthesized by the endocrine X/A-like cells of the fundus mucosa representing about 20% of gastric mucosal cells in humans [(2)]. Circulating ghrelin consists of more than 90% of desacyl ghrelin and less than 10% acyl ghrelin [(3)]. However, the acyl group of ghrelin is essential for its binding to growth hormone secretagogue receptor (GHS-R) and the concomitant activation of the inositol triphosphates/calcium pathway [(1)].In addition to the stomach [(4)] . ghrelin is expressed in many tissues such as duodenum, jejunum, ileum, colon, lung, heart, pancreas, kidney, testis, pituitary, and hypothalamus.

The physiological functions of Ghrelin include.

- Growth Hormone Releasing Activity
- Appetite Regulation
- Energy Homeostasis
- Gastric secretion and Gastro intestinal Motility
- Glucose Homeostasis
- Cardiovascular Functions
- Reproductive Functions. [(5)]

Infertility*:*

Infertility is the inability of a sexually active, non-contracepting couple to achieve spontaneous pregnancy in one year. Infertility affects both men and women.

Male fertility can be reduced as a result of

- congenital or acquired urogenital abnormalities.
- urogenital tract infections;
- increased scrotal temperature (e.g.as aconsequence of varicocele)
- endocrine disturbances;
- genetic abnormalities;
- immunological factors.

semen analysis reveals a decreased number of spermatozoa oligozoospermia, decreased permmotility asthenozoospermia, and many abnormal forms of sperm (teratozoospermia). These sperm abnormalities usually occur together and are called oligo-astheno-teratozoospermia (OAT) syndrome [(6)] .

Materials and methods*:*

Patients

Fifity blood samples and seminal fluids have been taken from infertiled men aged (25-50) years,in addition to twenty samples from apparently healthy pearsons .

Semen analysis (SA):

Every patient was asked to collect a fresh ejaculate into a sterile container.The ejaculate was allowed to liquefy for about 30 minutes. Using the WHO criteria (normal sperm count, >20 10^6/ml; normal sperm progressive motility ≥50%; and normal sperm morphology ≥ 30%) [(7)], Following macroscopic evaluation, sperm count and motility were evaluated by adding10 microliters of liquefied semen to Makler counting chamber under light microscopy (Nikon Co., Japan). For evaluation of sperm morphology,20 microliters of semen were placed on a clean microscope slide to make a smear. Each smear was fixed in methanol for 5 minutes. Sperm morphology was assessed on smears with Geimsa staining (Merck Chemical Co., Germany). The percentage of sperms with normal morphology was determined by assessing 100 sperms under oil immersion [(8)] .

Serum hormonal and lipids assessment

Blood samples were obtained following 12 h of fasting. The levels of serum cholesterol, LDL, HDL, and Triglyceride. Were measured. The measurements were done according to the manufacturing kitsm (BIOLABCO, France). The level of hormones, FSH, LH, Testosterone, prolactin TSH were measured for all patients and controls, according to the manufacturing kits (Monobind Inc lakeforst) ,CA92630 , USA) , and Ghrelin by (RAY Biotech, USA) using Elisa Technique.

Statistical analysis:

The statistic analysis was done using the statistic package for Social Science (SPSS) version (19),and Microsoft Excel (2007) software, Descriptive

statistics for all data of each set were expressed as Mean ± SD, student t-test, correlation would be significant if $p \leq 0.05$.

Results:

The results showed that the 50 infertiled men have significant differences in, FSH, LH, Prol, TSH, TG, HDL, VLDL, FBS, Ghrelin concentrations compared with healthy control groups ($p<0.05$), (Table 1) and there have no significant differences in the levels of testosterone, Cho, LDL-C in patients compare to control groups , (Table 2).

Table (1) The descriptive analysis including (Mean±SD) and p-values of, FSH, LH,TSH, prolactin, ghrelin, Tri, VLDL, HDL, FBS , for patients and control groups.

parameter	Groups	Mean±SD	p-value
FSH (ng/ml)	Control=20	7.89±3.87	p<0.05
	Patients=50	12.18±6.83	
LH (mIu/l)	Control=20	14.36±15.77	p<0.05
	Patients=50	5.31±1.81	
Prolactin (ng/ml)	Control=20	4.89±0.29	p<0.05
	Patients=50	13.07±11.59	
TSH (mIu/ml)	Control=20	1.51 ± 0.15	p<0.05
	Patients=50	2.40 ± 0.91	
Ghrelin (ng/ml)	Control=20	54.33 ± 5.54	p<0.05
	Patients=50	61.76±13.52	
TG (mg/dl)	Control=20	107.83±21.08	p<0.05
	Patients=50	142.00 ±67.00	
HDL (mg/dl)	Control=20	47.83 ± 6.43	p<0.05
	Patients=50	40.21 ±6.65	
VLDL (mg/dl)	Control=20	21.67 ± 4.35	p<0.05
	Patients=50	13.37 28.37±	
FBS (mg/dl)	Control=20	7.50 ± 7.588	p<0.05
	Patients=50	103.75 ± 33.04	

Table (2) The descriptive analysis including (Mean±SD) and p-values of testosteron , Cho , and LDL

parameter	Groups	Mean±SD	p-value
Testosteron ng/ml	Control=20	5.38±0.97	*P>O.O5*
	Patients=50	4.19±0.33	
Cho mg/dl	Control=20	181±21.68	*P>O.O5*
	Patients=50	169.28±39.28	
LDL mg/dl	Control=20	114.67± 25.78	*P>O.O5*
	Patients=50	102.35± 31.8	

Discussion:

Ghrelin activity at the pituitary level is not fully specific for GH, because it also includes stimulatory effects on both the lactotroph and corticotroph systems [9] .

In the present study, gonadotropin (FSH and LH) levels were significantly elevated in infertiled men when compared with the levels in fertiled control. These results are in agreement with the studies of Sulthan *et al.* [10]. Zabul *et al.* [11], Weinbaurer and Nieschlag [12],and Subhan et *al.*[13] who showed elevated levels of both follicle stimulating hormones(FSH),and luteinizing hormones(LH), in infertiled males.

The triglyceride(TG), VLDL, Concentrations were significantly elevated in infertiled men compared with the levels of fertiled control. These results were in agreement with the study of Vigron *et al* [14]. Ergün ***et al*** [15], Who found that increased serum total triglyceride and VLDL-c values had deleterious effects on spermatogenesis.

The Concentration of HDL-C was significantly elevated in infertiled men compared with the levels of fertiled control. These results are in agreement with the study of Padron ***et al*** [16], who reported a positive correlations between serum HDL-c levels, sperm density and viability in males.

There was a significantly elevation in FBS concentrations in infertiled men compared with the levels of fertiled control. These results are in agreement with the study of Rato***et al*** [17], and Scarano***, et al*** [18], who reported that the diabetic individuals are known to have a decrease in sperm motility and viability, and an increase in the percentage of abnormal spermatozoa.

Ghrelin levels were significantly elevated in infertiled men compared with the fertiled control .These results are in agreement with that of Furuta ***et al*** [19], who reported that ghrelin inhibits the secretion of LH and FSH. The effect might be exerted directly through GnRH-LH and GnRH-FSH axis or indirectly through corticotrophic releasing hormone(CRH) , and in agreement with the studies of Kluge ***et al*** [20], Lanfranco ***et al*** [21], who found that ghrelin inhibits the pulsatile LH secretion, and Barreiro *et al* [22], who demonstrated that ghrelin expression depends on the stimulatory effect of LH. El Eshmawy ***et al*** [23], reported that there was a negative effect of ghrelin on testosterone, luteinizing hormone and follicular stimulating hormone levels which were also seen in humans. In fact, lower ghrelin levels have been shown in hypogonadal men compared with weight-matched eugonadal men or normal weight control.

Testosterone level has no elevation in infertiled men compared with the fertiled control. These results are in agreement with the study of Smith *et al* [24], and Subhan *et al* [13] .

There was no significant differences in concentrations of Cholesterol in infertiled men compared with fertiled control. These results were in agreement with the study of Yamamoto ***et al*** [25] , who found that only high level of cholesterol affected the sperm motility in rabbits .

There was no significant differences in LDL-C concentrations in infertiled men compared with fertiled control. These results were in agreement with the study of Khalili **et al** [26] .who reported that the abnormal level of LDL-c was not involved with alterations in sperm parameters.

1.Correlations between cholesterol and other parameters.

Pearson correlative coefficients revealed a significant positive correlations between Cho, VL

DL and TG (r=**0.377, r=0.375)** respectively. Fig (1,2)

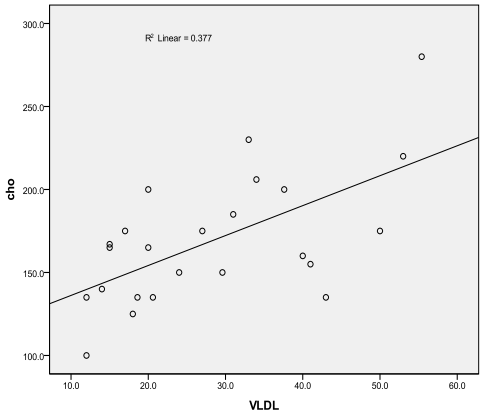

Figure (1) Correlation between cholesterol and VLDL concentration.

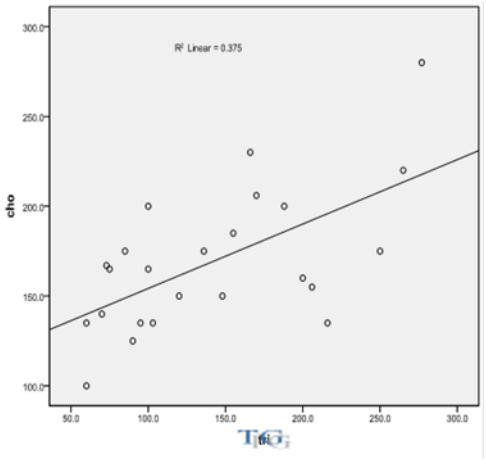

Fig (2) Correlation between cholesterol and TG concentration

2-Correlations between Triglyceride and Very low density lipoprotein concentrations .

Pearson correlative coefficients revealed a significant positive correlation between TG andVL DL**. (**r=1.000). Fig(3).

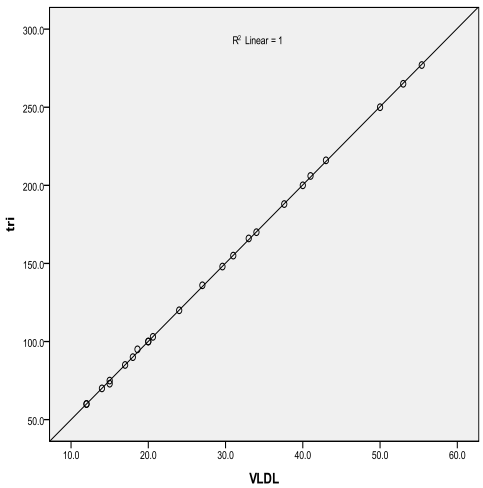

Fig (3) Correlation between triglycerid and VLDL concentration

3-Correlations between the concentration of Low density lipoprotein and Cho**.**

Pearson correlative coefficients revealed a significant positive correlations between LDL , and cho (r=0.868,**)** Fig (4).

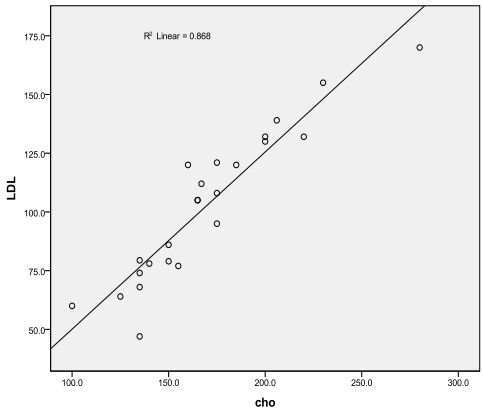

Fig (4) Correlation between LDL and Cho concentration.

4-Correlations between concentration of TSH and F.B.S.

Pearson correlative coefficients revealed a significant negative correlations between TSH, F.B.S. (r=0.199) Fig(5).

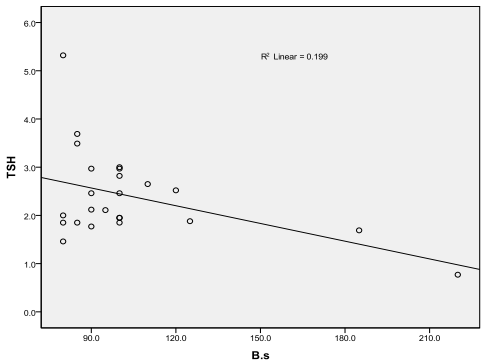

Fig (5) Correlation between TSH and F.B.S concentration

5- Correlations between FSH and F.B.S concentrations.

Pearson correlative coefficients revealed a significant positive correlation between FSH and F.B.S concentrations (r=0.282) . Fig(6).

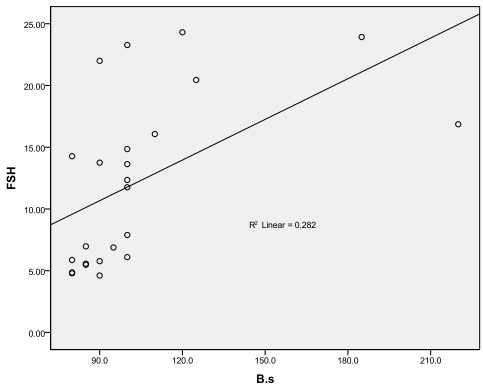

Fig (6) Correlation between FSH and F.B.S concentration

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تاثير هورمون الكرلين على الهورمونات الجنسية للرجال المصابين بالعقم

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الملخص

صممت الدراسة الحالية لتقييم تاثير هرمون الكرلين على الهرمونات الجنسية قبل الهرمونات المحفزة للقند والهرمونات اللوتينية والتيستوسترون والبرولاكتين في الذكور العقماء. ان تخليق الحيامن غير الطبيعي غالبا مايرتبط مع تغيرات الكونادوتروبين والتسيتوسيرون في الدم. ان مستوى الهرمونات المحفزة للقند والهرمونات اللوتينية والتسيتوسيران قد تم تقديرها في خمسين عينة لاشخاص عقماء وقد اثبتت النتائج ان هناك زيادة معنوية ($p< 0.05$) في مستوى هرمون الكرلين والهرمونات المحفزة للقند والهرمونات اللوتينية والهرمونات المحفزة للدرقية والبرولاكتين وكذلك في مستوى السكر ثلاثي الكليسيروات وكل من البروتينات الدهنية عالية الكثافة HDL-c وواطئة الكثافة VLDL-c في كل العينات الماخوذة من الاشخاص العقماء مقارنة مع مجموعة السيطرة (n=20) . اضافة الى ذلك فان النتائج اوضحت عدم وجود فروق معنوية في مستويات التسينوسترون والكولسيزول والبروتينات الدهنية واطئة الكثافة LDL-c في الاشخاص العقماء مقارنة مع غير العقماء.